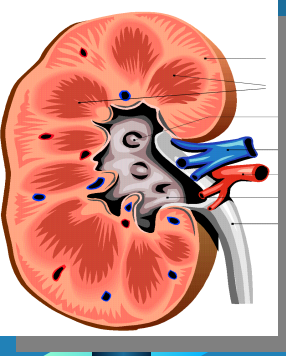


WRAMC
Walter Reed Army Medical Center
NEPHROLOGY SERVICE

The Renal Biopsy in High Risk Patients with Medical Diseases of the Kidney

Kevin C. Abbott, MAJ, MC, FACP

An Interdisciplinary Conference of Nephrology,

Radiology, Urology, Organ Transplantation,

Pediatrics and Pathology

ARMY MEDICINE
CARING BEYOND THE CALL OF DUTY

Purpose of today's talk

- The approach to high risk patients for patients needing renal biopsy has been changing rapidly, as new techniques develop.
- These changes have led to some differences of opinion between services.
- Our goal today is to learn from each other and lay groundwork for a consensus approach to the management of these patients.

Objectives

- Understand the essential history of the renal biopsy
- Know what constitutes high risk for patients undergoing renal biopsy.
- Know the difference between absolute and relative contraindications to renal biopsy.

Objectives (Cont'd)

- Know the current and emerging techniques for this procedure
- Understand what constitutes adequate tissue for diagnosis
- Know how to diagnose and manage complications of this procedure
- Discuss an institution specific approach to these patients

Outline

- Brief History of the Renal Biopsy in Medical Diseases of the Kidney
- Brief overview of current approach to low risk patients
- Approaches to high risk patients (and who *IS* high risk?):
  - medical
  - technical

Outline (Cont'd)

- Comparison of adequacy, risk and complexity (i.e., cost) for the various approaches
- Diagnosis and Management of Complications
- Will focus an area's discussion on prospective trials if they exist, brief discussion of retrospective trials and case series/reports.

Historical Background

- Percutaneous kidney biopsy (of palpable tumors) first performed by Ball in 1934 in London (1)
- Iversen and Brun in Denmark, 1951, first to perform needle kidney biopsy for medical disease (Ibid)

1) Renal Biopsy: An Historical Perspective, Conrad R. Pirani, from Renal Biopsy Interpretation, Silva, D'Agati, Nadasdy eds, Churchill Livingstone, New York, c 1996.

Historical Background (Cont'd)

- Introduced in 1953 to US by Parrish and Howe of the Washington, DC VA Hospital (Ibid).
- At Georgetown, Dr. George Schreiner and colleagues established one of the first clinico-pathology working groups (Ibid).

Historical Background (Cont'd)

- In Chicago in 1954, Kark and Muehrcke used a Franklin modified Vim-Silverman needle and positioned the patient prone (rather than standing), using the "blind approach" (and later IVP) localize the kidneys and procure renal tissue (Ibid). This technique would remain prevalent for more than 40 years!

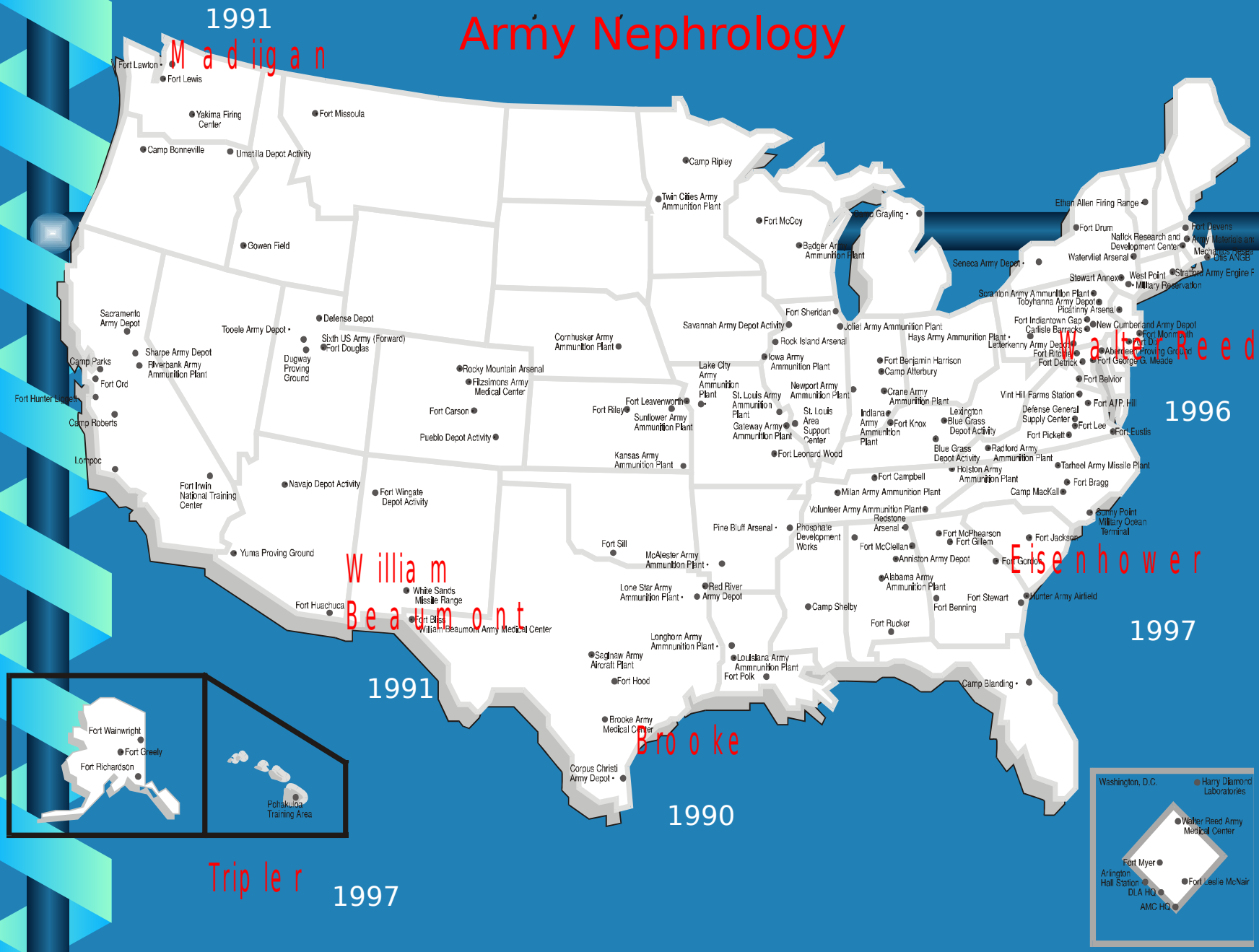
Historical Background (Cont'd)

- Various imaging modalities, such as IVP, fluoroscopy, renal scintigraphy, and ultrasound were also used to localize the kidneys.
- Of these, ultrasound was found the localize the lower pole (the lowest risk approach and highest yield for glomeruli) the best. Also not affected by renal failure. Systematically compared by Bolton et al (1).

Historical Background (Cont'd)

- Two other key events developed later:
  - Real-time ultrasound guidance was used to visualize a Tru-Cut needle as it entered the kidney (1) at Rush-Presbyterian in Chicago by Birnholz et al.
  - Adopting techniques used for liver biopsy, a spring-loaded biopsy gun (18g) was used to obtain renal tissue at Wilford Hall Medical Center in San Antonio (2). Many other subsequent reports were published (3).

Army Nephrology

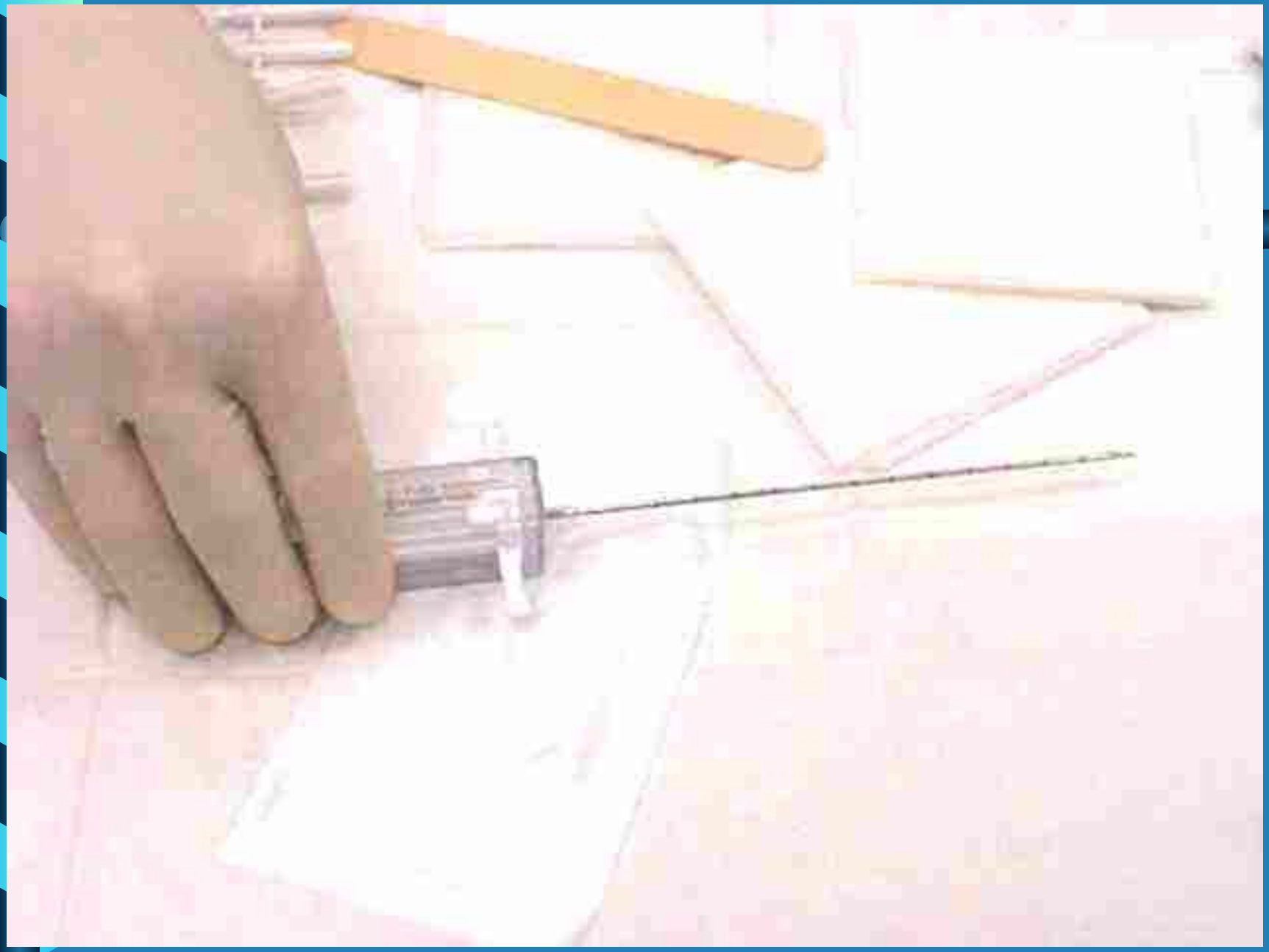


Historical Background (Cont'd)

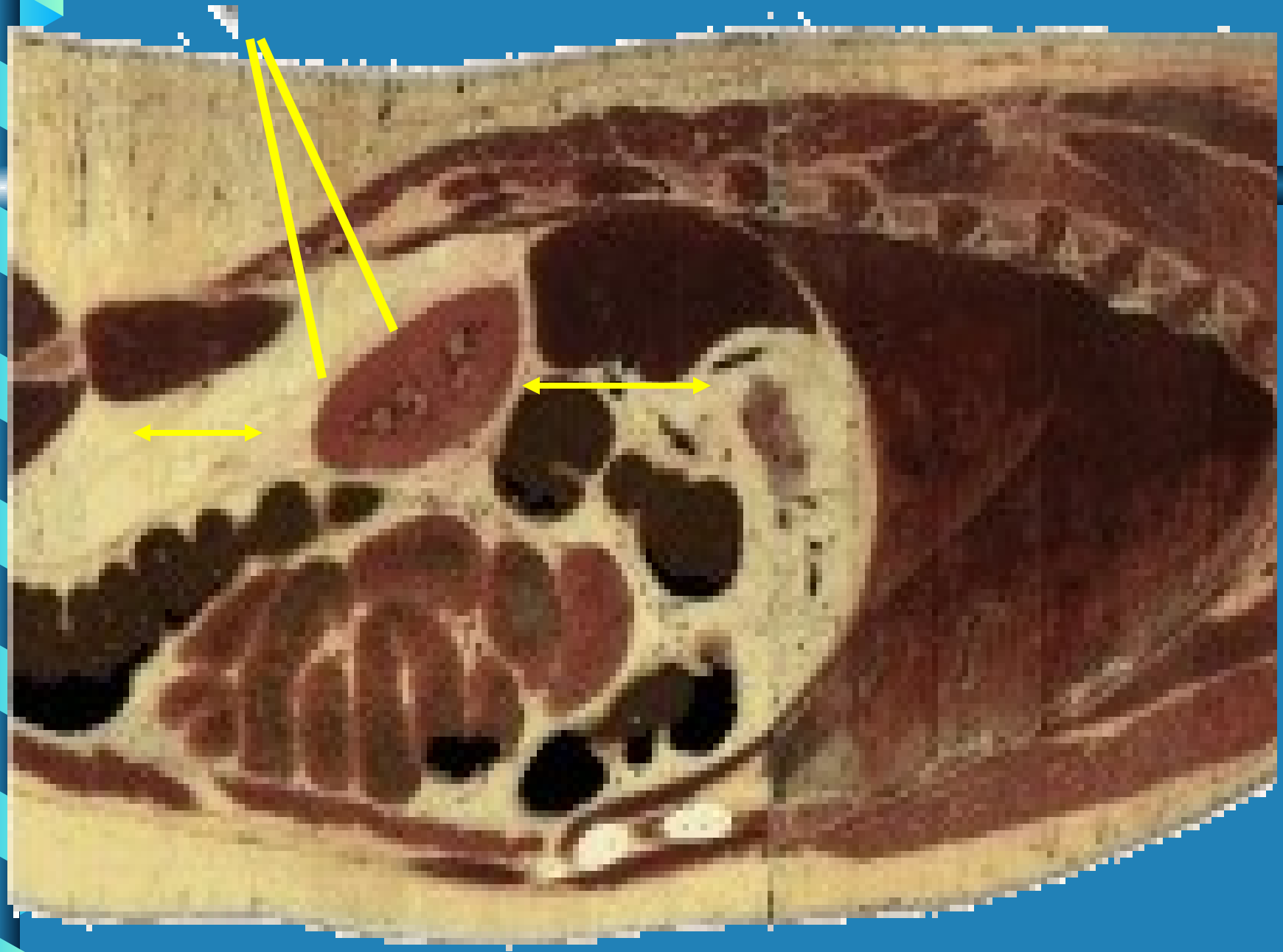
- Although initially more labor-intensive, the time the needle spent in the kidney was shortened.
- Also of importance--especially for non-surgeons-- this technique required less dexterity to obtain good samples.

Current Practice

- Despite the lack of well designed clinical trials with supporting evidence, these techniques have proliferated and become the de facto standard for kidney biopsies in the US (although exact practice patterns are difficult to quantitate because they are not tracked nationally.)

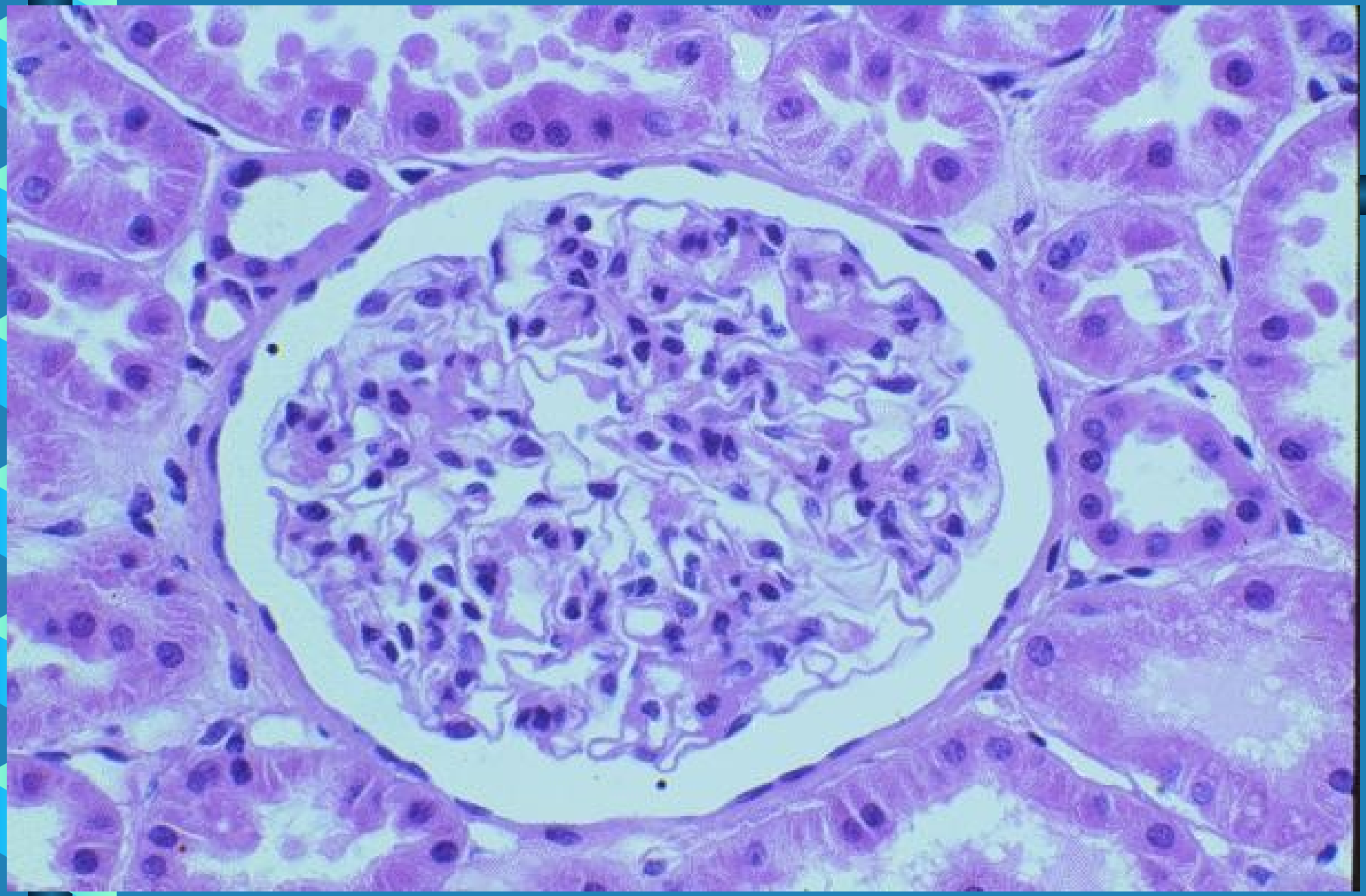


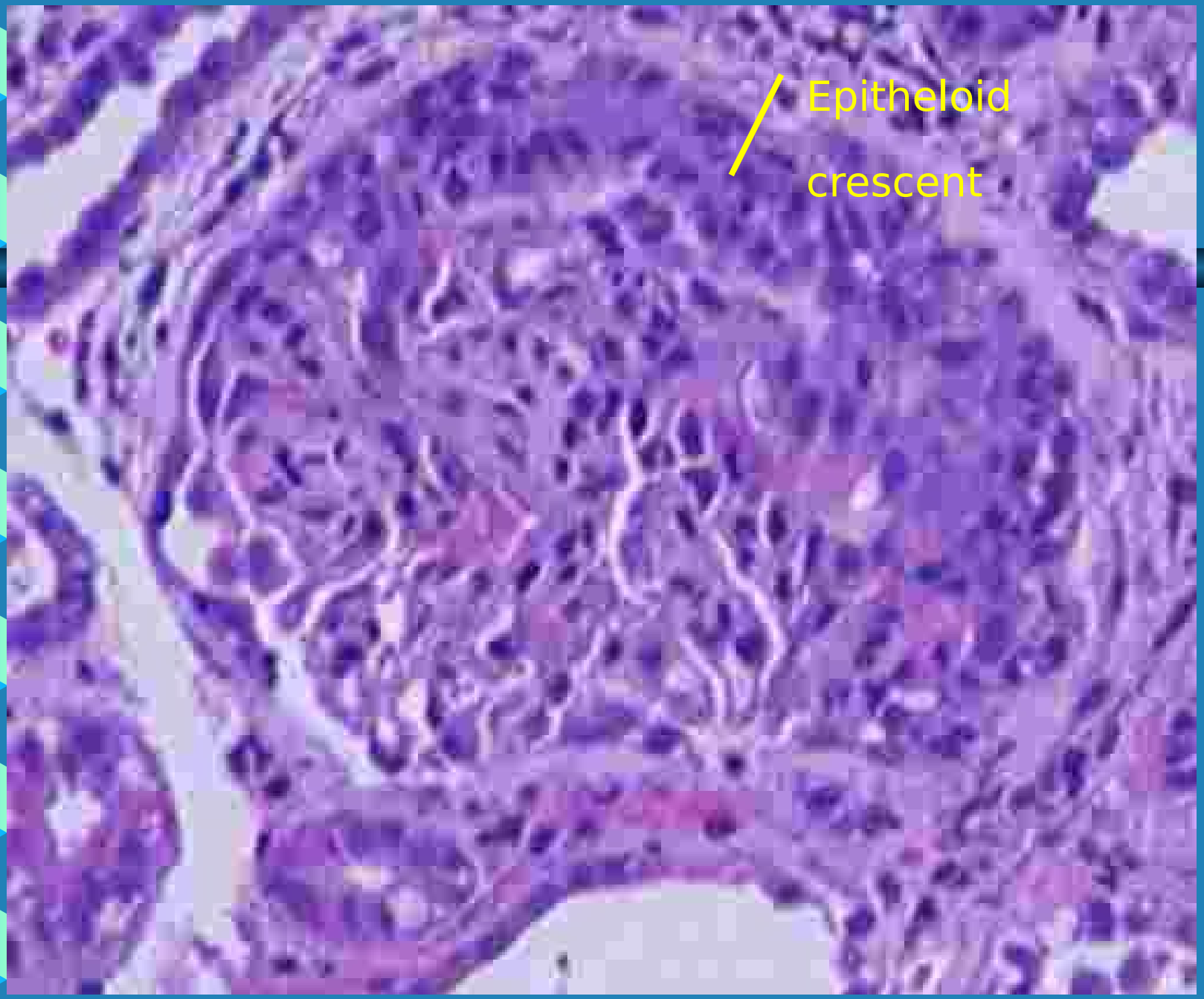
Transducer



Movie of renal ultrasound

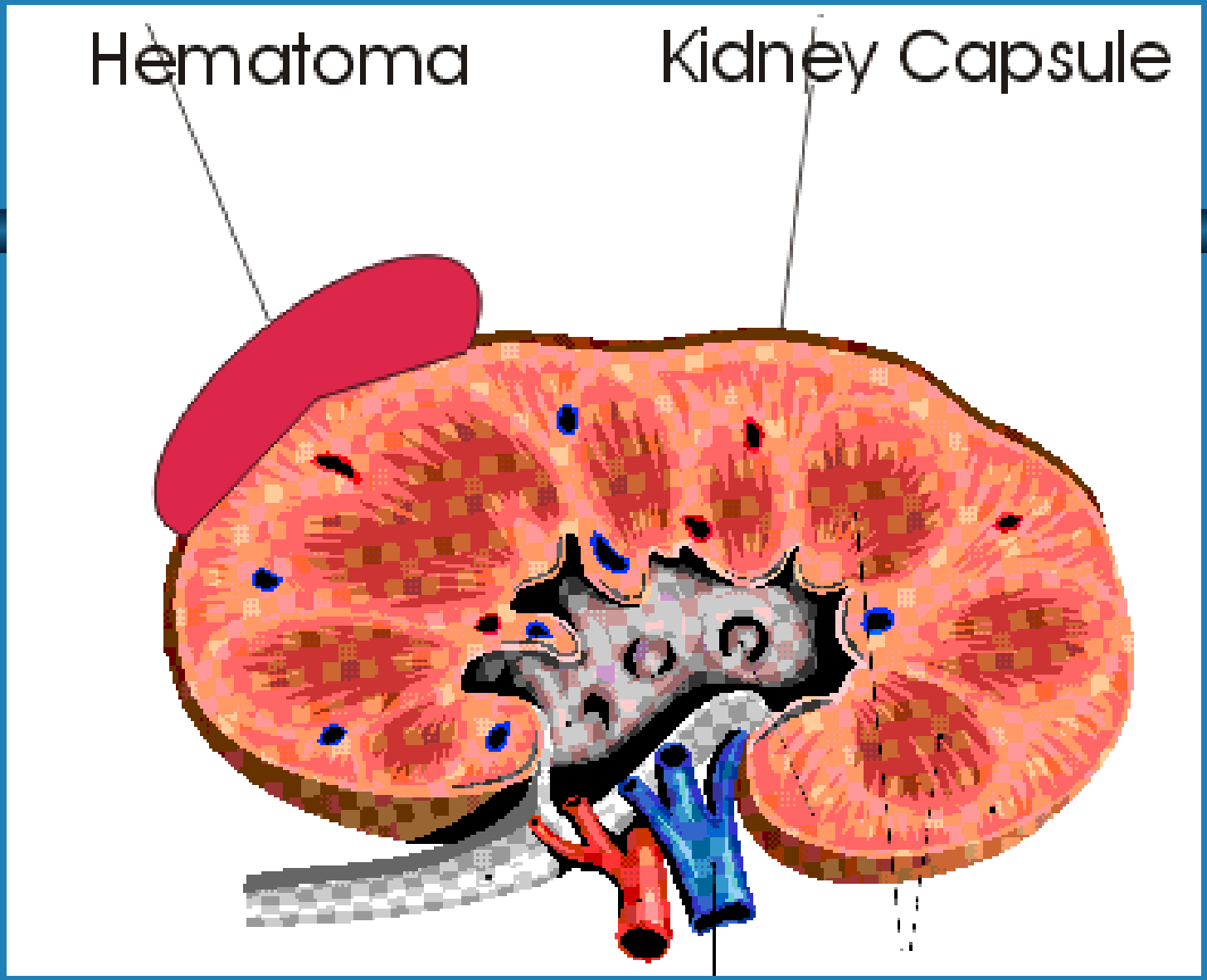
- Movie

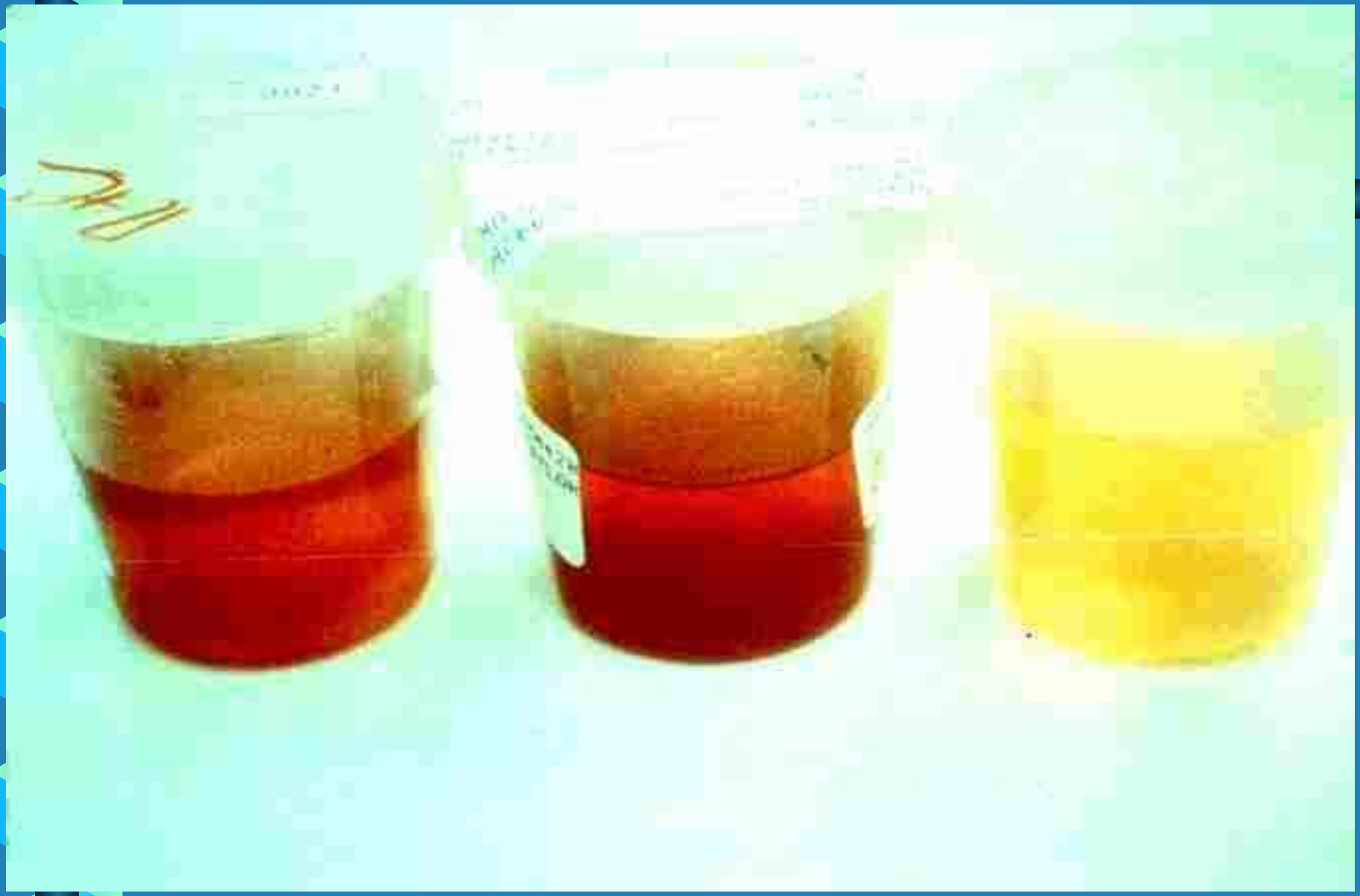


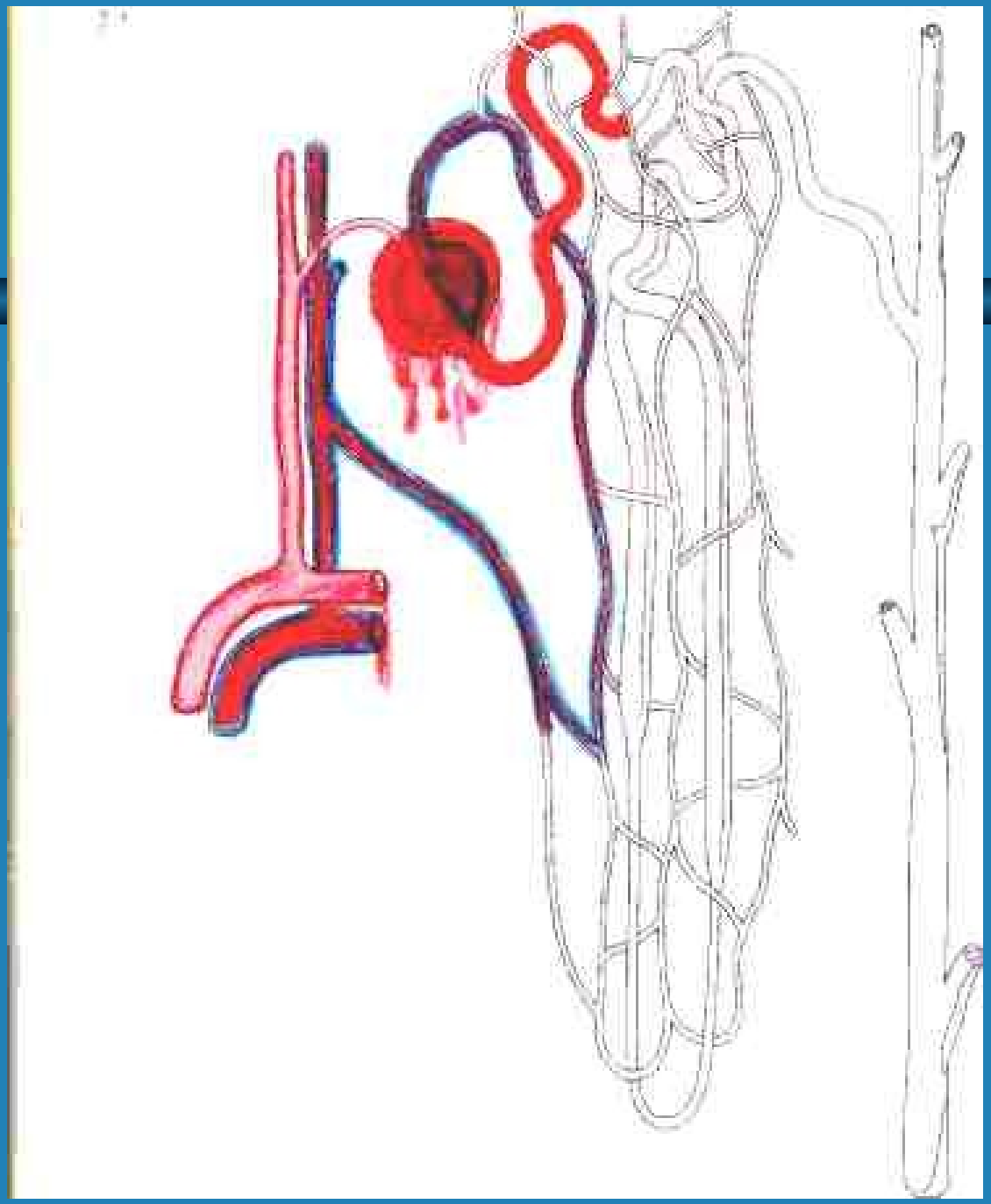

Epitheloid
crescent

List of Diagnoses from Renal biopsies, WRAMC, 1994-1998

Re		
Final Diagnosis2	Final Diagnosis	Total
amyloidosis	amyloidosis	1
C1q nephropathy	C1q nephropathy	1
chronic sclerosing GN	chronic sclerosing GN	2
CRF	CRF	1
CyA/FK toxicity	CyA/FK toxicity	1
diabetic nephropathy	diabetic nephropathy	8
FSGS	FSGS	24
Hereditary Nephritis	Hereditary Nephritis	1
HIV nephropathy	HIV nephropathy	2
hypertensive nephrosclerosis	hypertensive nephrosclerosis	2
IgA nephropathy	IgA nephropathy	10
IgM nephropathy	IgM nephropathy	6
immune complex GN	immune complex GN	1
Inadequate	Inadequate	1
inadequate	inadequate	4
interstitial nephritis	interstitial nephritis	4
membranous - idiopathic	membranous - idiopathic	6
membranous - secondary	membranous - secondary	3
mesangial GN	mesangial GN	3
minimal change dz	minimal change dz	4
multiple myeloma	multiple myeloma	4
N/A	N/A	15
other (enter comment)	other (enter comment)	2
PAN - microscopic	PAN - microscopic	1
Rejection		12
SLE		10
Grand Total		129


Hematoma
Kidney Capsule





Current Practice

- CT-Guided biopsy also has a long track record. It does not allow direct visualization, but can allow successful percutaneous biopsy when kidney position does not support ultrasound guided biopsy (ie, if the kidnes do not fall below the ribs with inspiration).

Current Practice--comparison of manual vs. automated biopsies

- Only one study has compared manual vs. “automated” renal biopsies in a prospective fashion (1).

Current Practice--comparison of manual vs. automated biopsies

- Population: 166 patients who underwent percutaneous renal biopsy at Suwon, Korea (Ajou University Medical Center) were randomized in a prospective trial from June 1994 to February 1997.

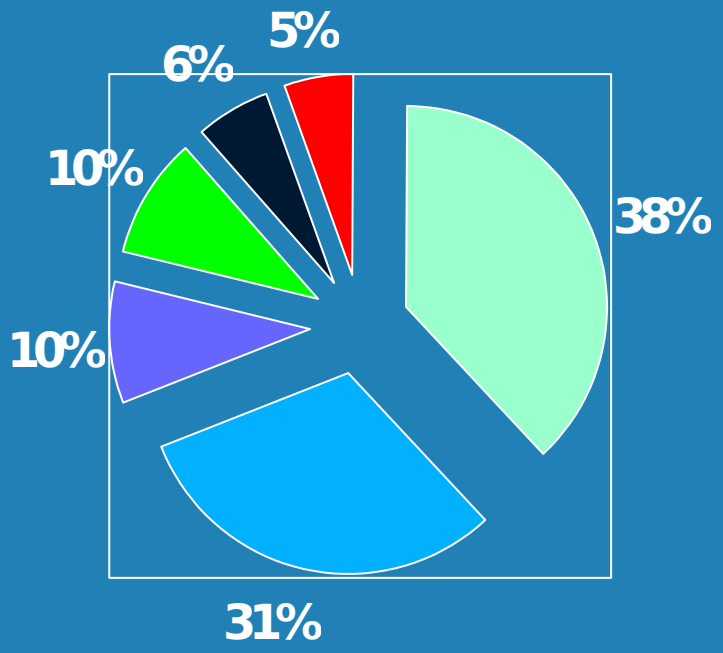
Current Practice--comparison of manual vs. automated biopsies

- Groups:
  - 67 underwent manual Tru-Cut 14 G needle biopsy under ultrasound localization, but not real-time guidance.
  - 99 underwent biopsy with 18 G automated gun (Pro-Mag 2.2 biopsy system) under real-time guidance.
- All groups had left kidney biopsied

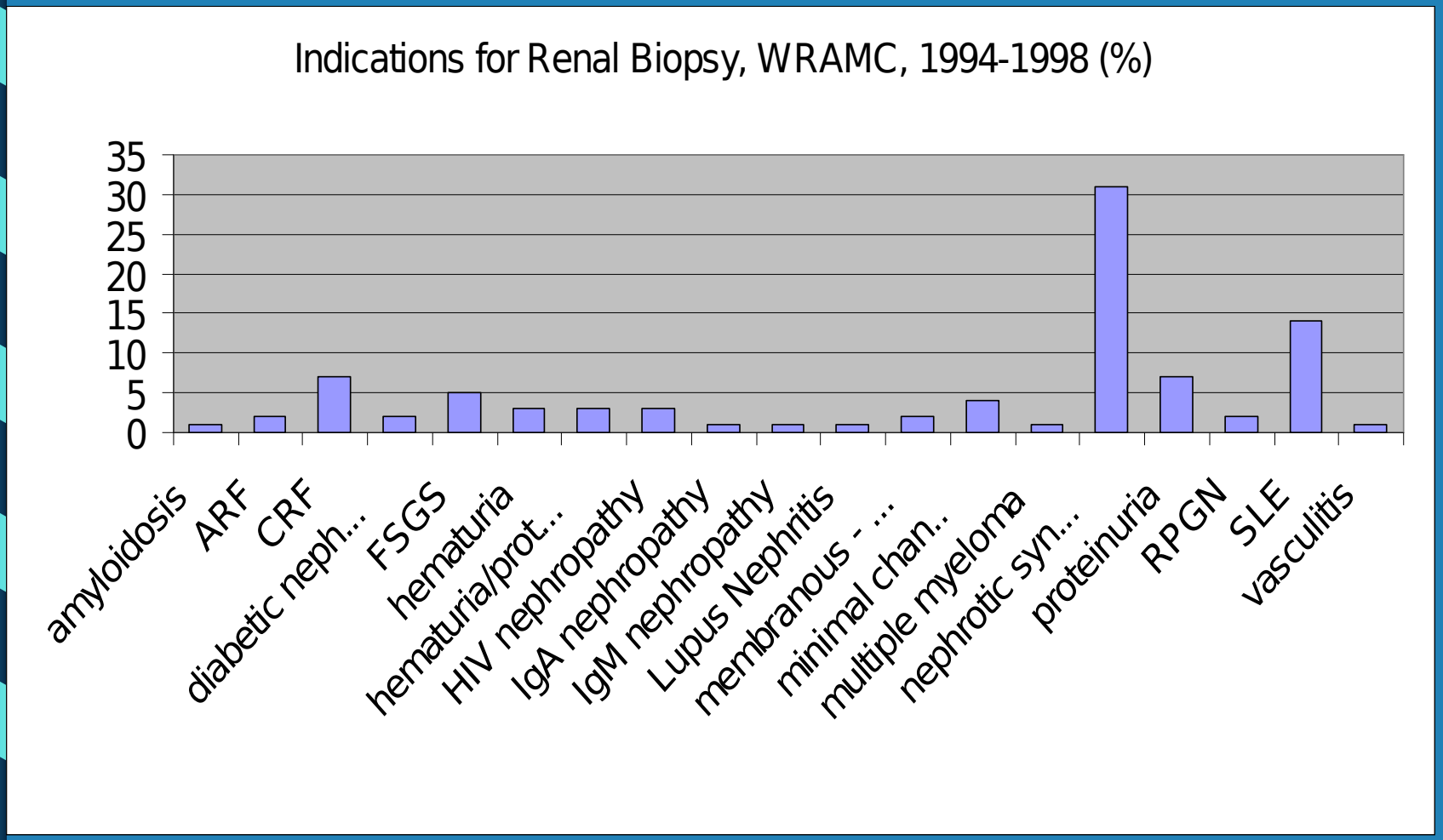
Current Practice--comparison of manual vs. automated biopsies

- Tru-Cut biopsies performed by one nephrologist
- Automated biopsies performed by several physicians including trainees under supervision.
- At least two cores obtained.
- Adequacy defined as at least five glomeruli (analyzed immediately by pathology, technique not stated).

Current Practice--comparison of manual vs. automated biopsies



Current Practice: WRAMC

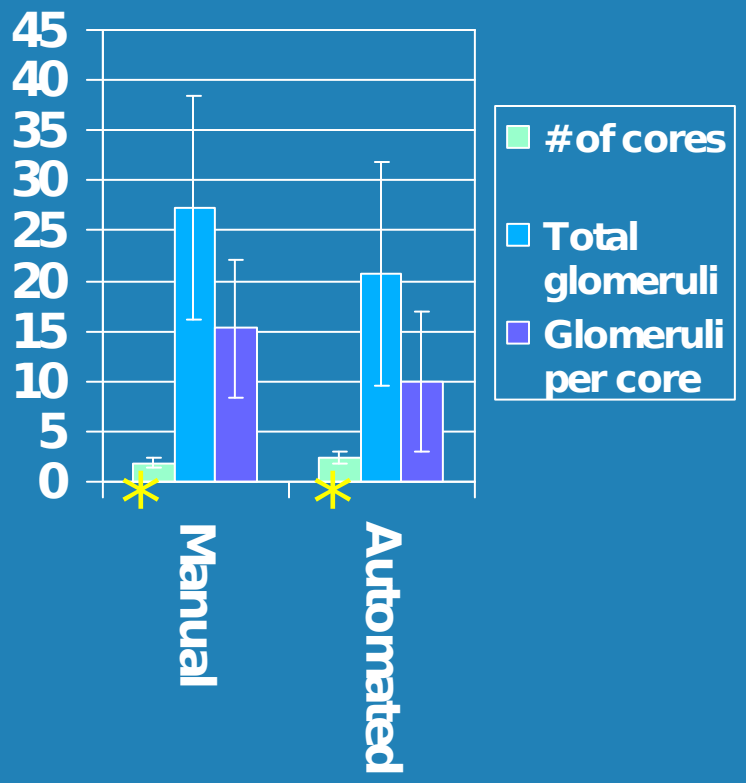


Current Practice--comparison of manual vs. automated biopsies

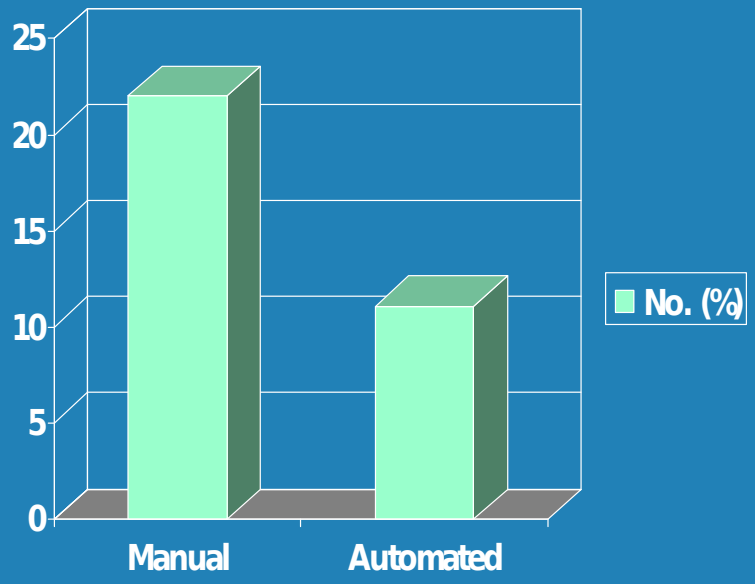
- Groups were comparable in gender ratio (1.15:1 vs 1.23:1 males to females), age (35 yrs), coagulation and hematocrits, and blood pressures (which were 127/81 and 126/80 respectively--use of antihypertensive medications not mentioned).

Current Practice--comparison of manual vs. automated biopsies

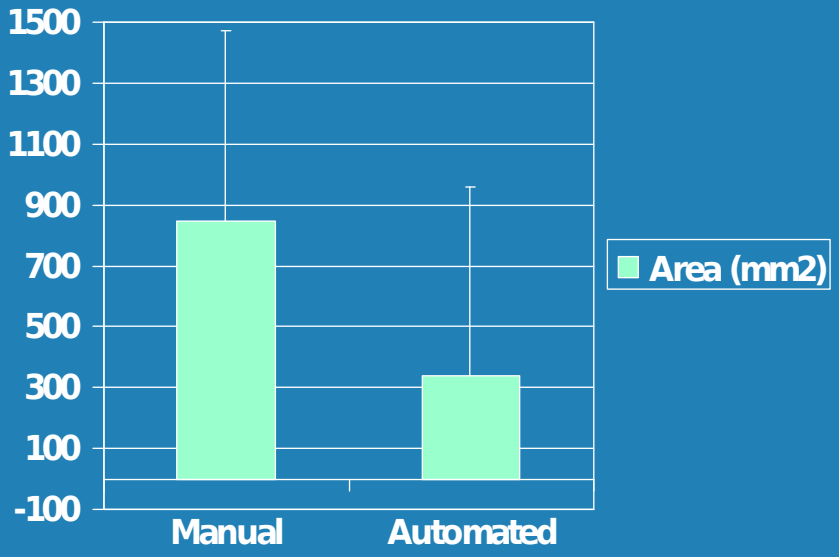
- Differences between the two techniques.
- *=p<0.001 for the number of cores (1.88 for manual to 2.37 for automated)
- Significantly greater total glomeruli (p 0.017) and glomeruli per core (p 0.026) for manual biopsy



Current Practice--comparison of manual vs. automated biopsies



No. of perirenal hematomas (%)



Area of perirenal hematomas (mm2)

Current Practice--comparison of manual vs. automated biopsies

- Hematocrit (but not hemoglobin) values decreased significantly after the biopsy in the manual group (34.9 to 34.0, P=0.03) while no significant change was seen in the automated group (35.1 to 34.7). It is doubtful these differences would be clinically important.

Current Practice--comparison of manual vs. automated biopsies

- One patient in each group was transfused PRBC's, in each case BEFORE the biopsy, because hematocrits were already low. There were no deaths or other severe complications.

Current Practice--comparison of manual vs. automated biopsies

- Many retrospective studies have demonstrated lack of significant differences in complication rates and tissue adequacy between manual and automated techniques.
- A review summarizes most of the major reports (including pediatric and transplant) listed 3 AVF's and 1 death in 4834 reported biopsy series (1)

Current Practice--does size matter?

- Only one study has compared the effect of two different needle gauges when biopsy technique was otherwise held constant (in this case, CT guided biopsy), although in a retrospective fashion (1).

Current Practice--does size matter?

- Bard Biopty guns were used
- Major hemorrhagic complications occurred in 2.7% of the 18g group and 3.4% of the 14 g group (insig).
- Mean intact glomeruli per specimen were 10.7 with 18g and 13.7 with 14g (insig).
- Tissue recovery was 96% and 99% respectively.

Current Practice: inpatient or outpatient?

- Renal Biopsy as an outpatient procedure (1): Prospective study of 350 patients in Australia “offered the choice” between inpatient (strict bedrest for 24 hours) and outpatient management (allowed to leave after 8 hours) of renal biopsy between 1992 and 1994.
- Median age was 38.5 yrs
- Indications for biopsy not listed

Current Practice: inpatient or outpatient?

- Preponderance of females because of association with obstetrics hospital.
- “High risk” patients were excluded: Scr >2.7 mg/dl, or with renal transplant, or already in hospital.

Current Practice: inpatient or outpatient?

- Vim-Silverman needle was used with imaging by fluoroscopy or ultrasound, no real-time guidance.
- Complications were 2/118 (1.7%) for the outpatient group vs. 3/232 (1.3%) for the inpatient group.
- Longer term follow-up was not mentioned.

Current Practice: inpatient or outpatient?

- Power was 91% to detect a 10% (reasonable clinical difference) between groups, indicating adequate sample size.
- No patients required transfusions and there were no deaths.
- They attributed their low rate of complications to aiming for the lateral border of the mid-pole of the kidney.

Current practice: how long to observe?

- Mounting pressure by managed care to not only switch to outpatient management but to decrease period of observation to 6-8 hours (ie, a business day or one nurse's shift).
- Is it safe?

Current practice: how long to observe?

- 394 patients underwent 14 G Trucut (225 patients) or later 14 G automated needle biopsy between 1983 and 1995 (1).
- Imaging done by real time ultrasound
- Average age was mid 40’s. Males were the minority (<40%).
- Scr was 2.9 mg/dl for those with complications and 2.3 for those without.

Current practice: how long to observe?

- Total complication rate was 13%.
- 6.6% for minor complications (gross hematuria and perirenal hematomas that resolved).
- 6.6% for major complications (transfusion req bleed (22), invasive procedure needed (3), infectious complication).
- No deaths or nephrectomies

Current practice: how long to observe?

- Major complications identified in 46% of patients at <4 hrs, 79% at <8 hrs, and 100% at 12 hours.
- Thus, 20% of complications would have been missed by release at 8 hours.
- Authors still recommend 23 hour observation.

Current practice: how long to observe?

	Hours Post Biopsy				
	<4	5-8	9-12	13-24	>24
Minor complication (n)	12	3	3	1	1
Major complication (n)	11	8	5	0	0

Current practice: how long to observe: Pediatrics?

- A study of 177 percutanous renal biopsies in pediatric patients reported a 3.4% major complication rate and 14.1% minor complication rate. (1)
- All patients with major complications were diagnosed within 11 hours.

Contraindications (or, who IS at high risk?)

- Bleeding diathesis
  - Can usually be controlled prior to and for a few days following the biopsy
- Have previously recommended open biopsy with direct visualization if not controllable. Open biopsy has been done with mild sedation and local anesthetic (1).

Contraindications

- The risk of general anesthesia varies with ASA class. For ASA 2 (mild to moderate systemic disturbances, such as essential hypertension, mild diabetes or anemia) the death rate is 3/1000 (1).
- For Class 3 death risk is 1.8%, and 7.8% for Class 4.

Contraindications

- In the opinion of some (such as Dr. Modaio, in Renal Biopsy, Kidney Int, 38:529-543, 1990) the solitary kidney was thus a relative contraindication to percutaneous renal biopsy.
- The risks of anesthesia from an open procedure might be greater than the risk of nephrectomy from a closed procedure.
- The option of an open procedure under local anesthesia was not mentioned.
- Transvenous biopsy and other techniques were only beginning then.

Contraindications

- Unable to cooperate (in adults, these patients would not be biopsied unless judged incompetent with a consenting guardian. In children, sedation is generally used.)
- Single kidney
  - Risk of nephrectomy following renal biopsy reported at 5/8081 (1/1616) at the first ASN meeting (1968). Risk of death 1/2000 to 1/5000 (see references below)

Contraindications

- The other important contraindication is patients with end-stage or near end-stage renal disease with small kidneys. Significant complications were reported (5/29, 17%) in a study by Kropp et al (1). In these patients, Modaio still recommended open biopsy, although the need to biopsy such patients at all was questioned.

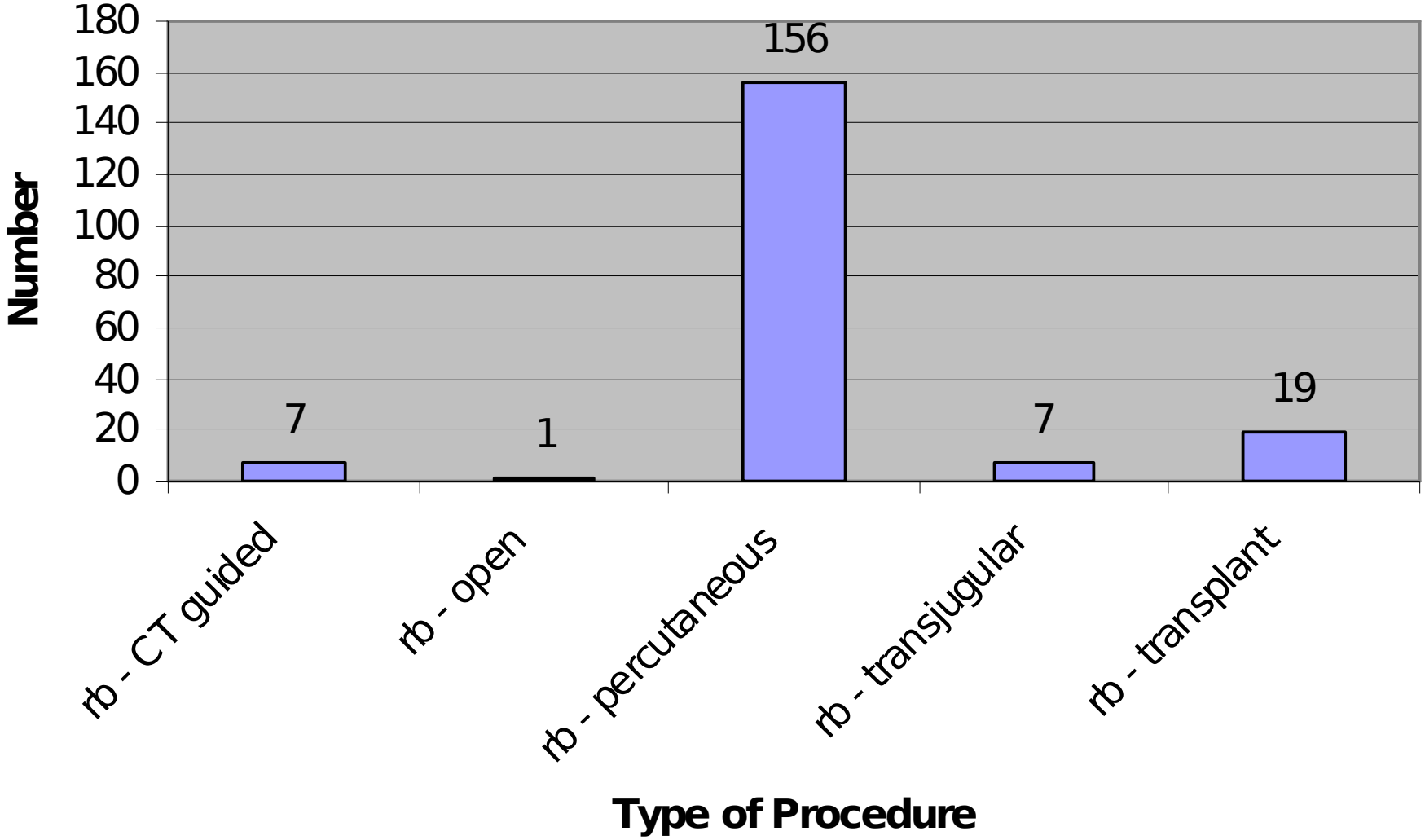
Contraindications (cont'd)

- Possible complications are certainly important to present to the patient, but are often hard for them to grasp.
- We have developed a tool to make this easier.

Approach to high risk patients: newer techniques

- Transjugular
- Laparoscopic
- Transfemoral
- Biopsy along the retrograde puncture line of the renal calyx

Renal Biopsy Techniques Used at WRAMC, 1992-1998



Newer techniques

- None of the following studies address the management of peri-procedure anticoagulation, I.e., heparin window, or just discontinuation of anticoagulation.
- At current remains individualized and opinion based
- This area is in need of further investigation.
- Recommendations from a recent review follow (next slide)

Recommendations for Perioperative anticoagulation in patients taking oral anticoagulants

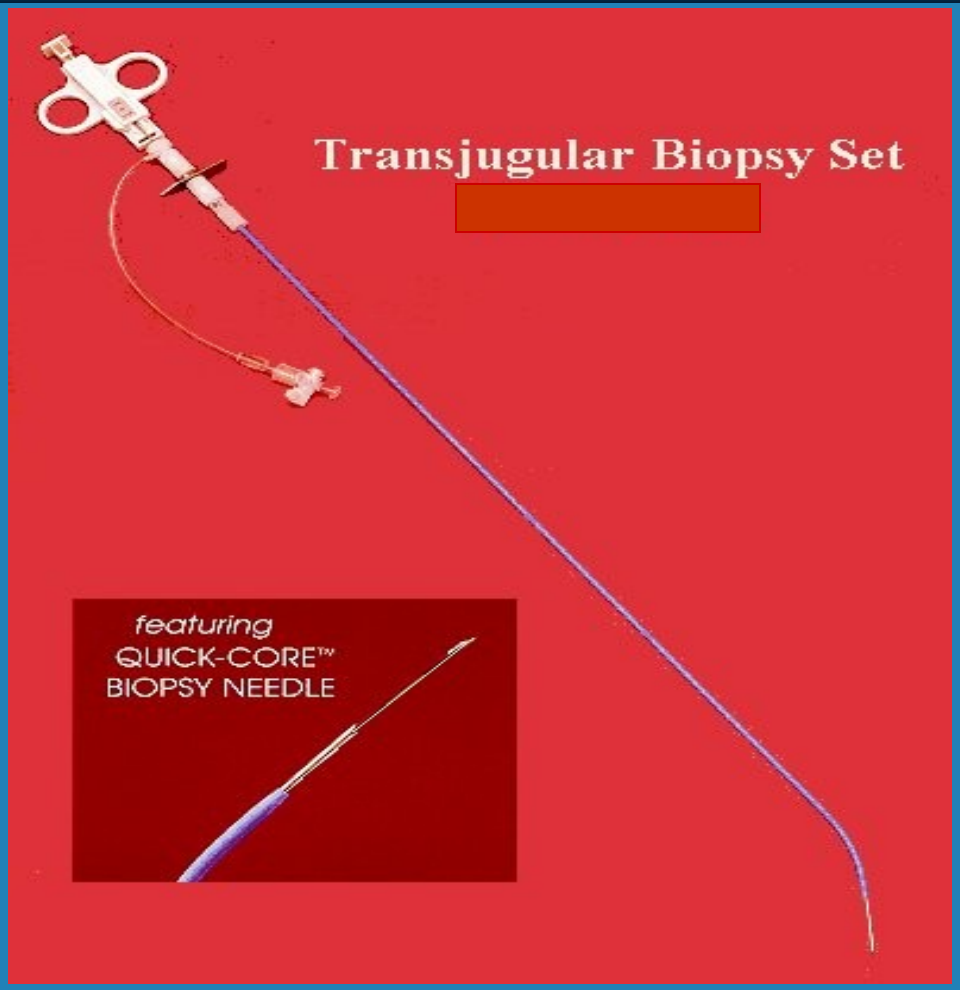
Indication	Before Surgery	After Surgery
Acute venous thromboembolism		
Month 1	IV heparin	IV heparin
Month 2 and 3	No change	IV heparin
Recurrent venous thromboembolism	No change	SC heparin
Acute arterial embolism	IV heparin	IV heparin
Mechanical heart valve	No change	SC heparin
Nonvalvular atrial fibrillation	No change	SC heparin

Adapted from Kearon D, Hirsh J. Current Concepts: Management of Anticoagulation before and after elective surgery. N Eng J Med 336(21):1506-1511, 1997.

Transjugular renal biopsy

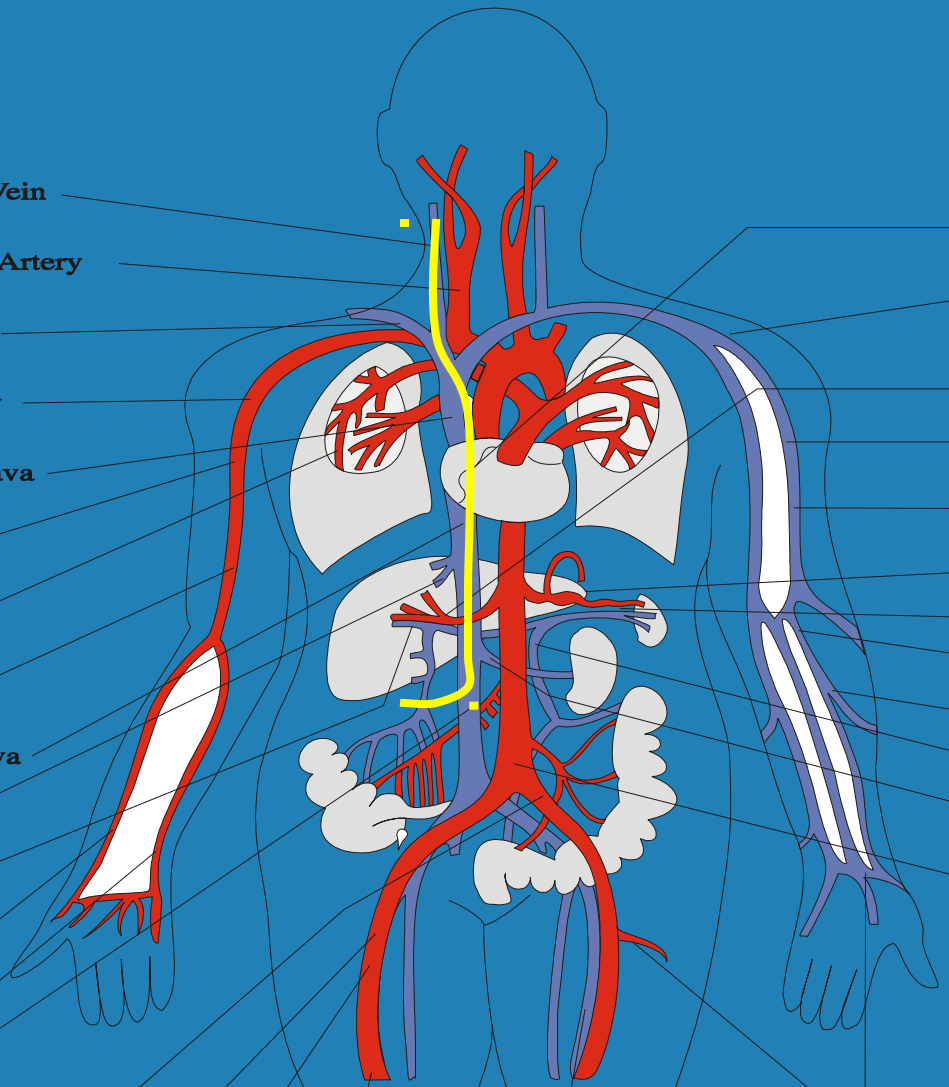
- Largest case series to date by Mal et al (1)
- Time frame not stated
- First determined the curvature and rigidity of the liver biopsy needle was compatible with biopsy of the right kidney (see following diagrams).

Transjugular renal biopsy

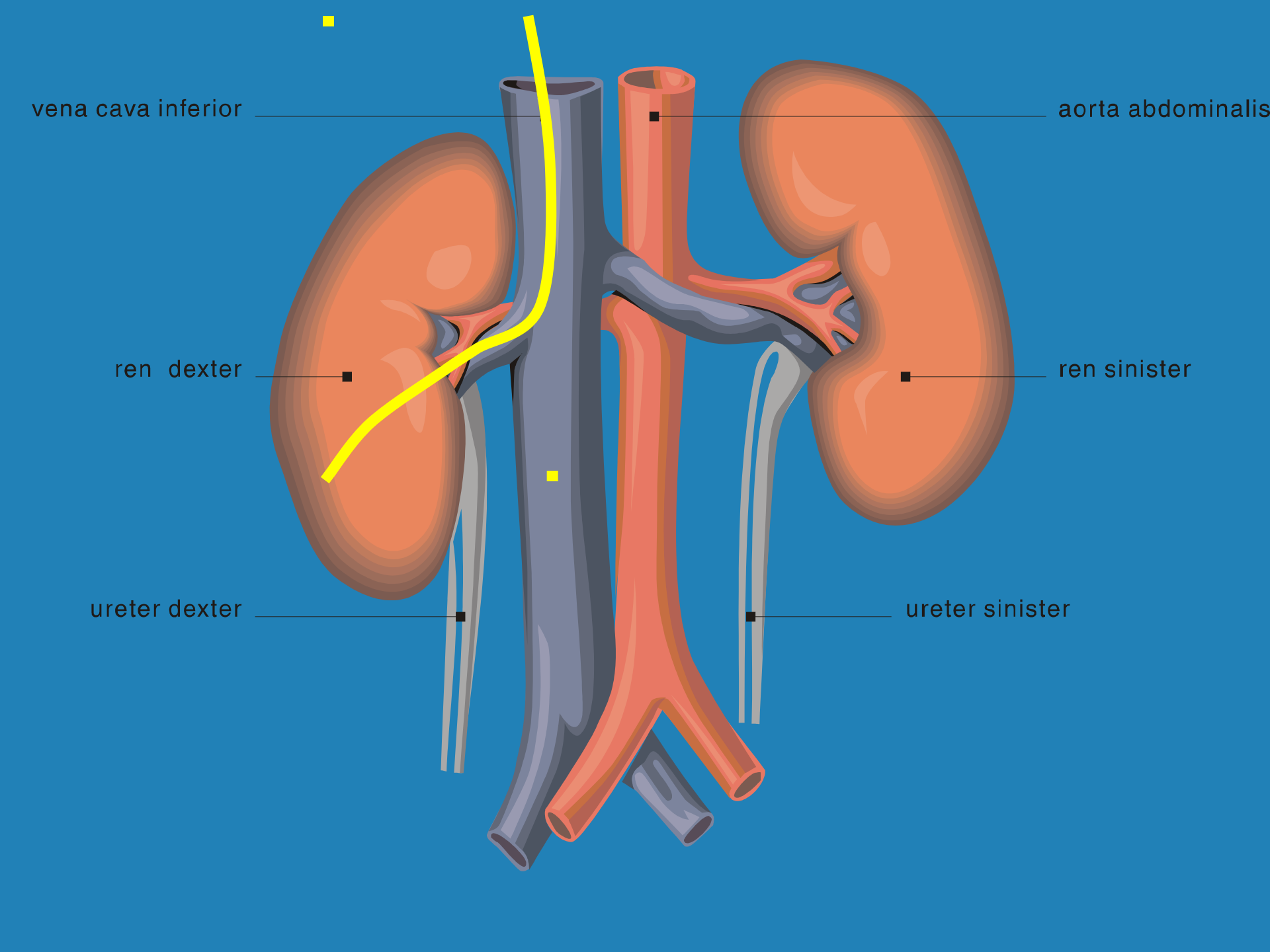


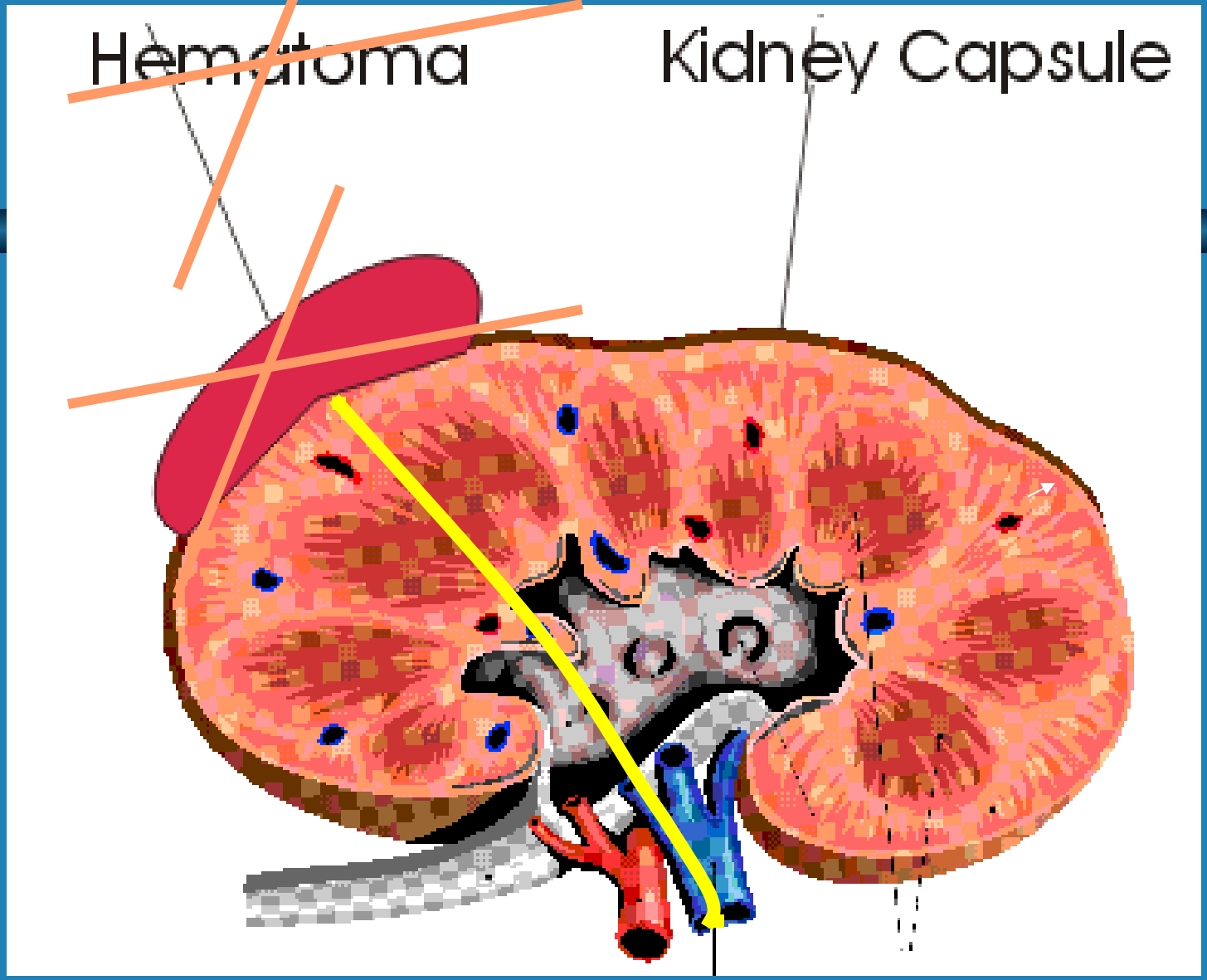
Blood Circulation

Principal Veins and Arteries



Internal Jugular Vein
Common Carotid Artery
Subclavian Vein
Subclavian Artery
Superior Vena Cava
Axillary Artery
Pulmonary Vein
Brachial Artery
Inferior Vena Cava
Hepatic Vein
Portal vein
Radial Artery
Ulnar Artery
Superior Mesenteric Artery
Common Iliac Artery
Internal Iliac Artery
External Iliac Artery
Femoral Artery
Great Saphenous Vein
Femoral Vein
Median Vein of Forearm
Abdominal Aorta
Renal Vein
Renal Artery
Radial Vein
Cubital Vein
Splenic Vein
Splenic Artery
Basilic Vein
Cephalic Vein
Common Hepatic Artery
Axillary Vein
Pulmonary Artery


vena cava inferior
aorta abdominalis
ren dexter
ren sinister
ureter dexter
ureter sinister


Hematoma
Kidney Capsule

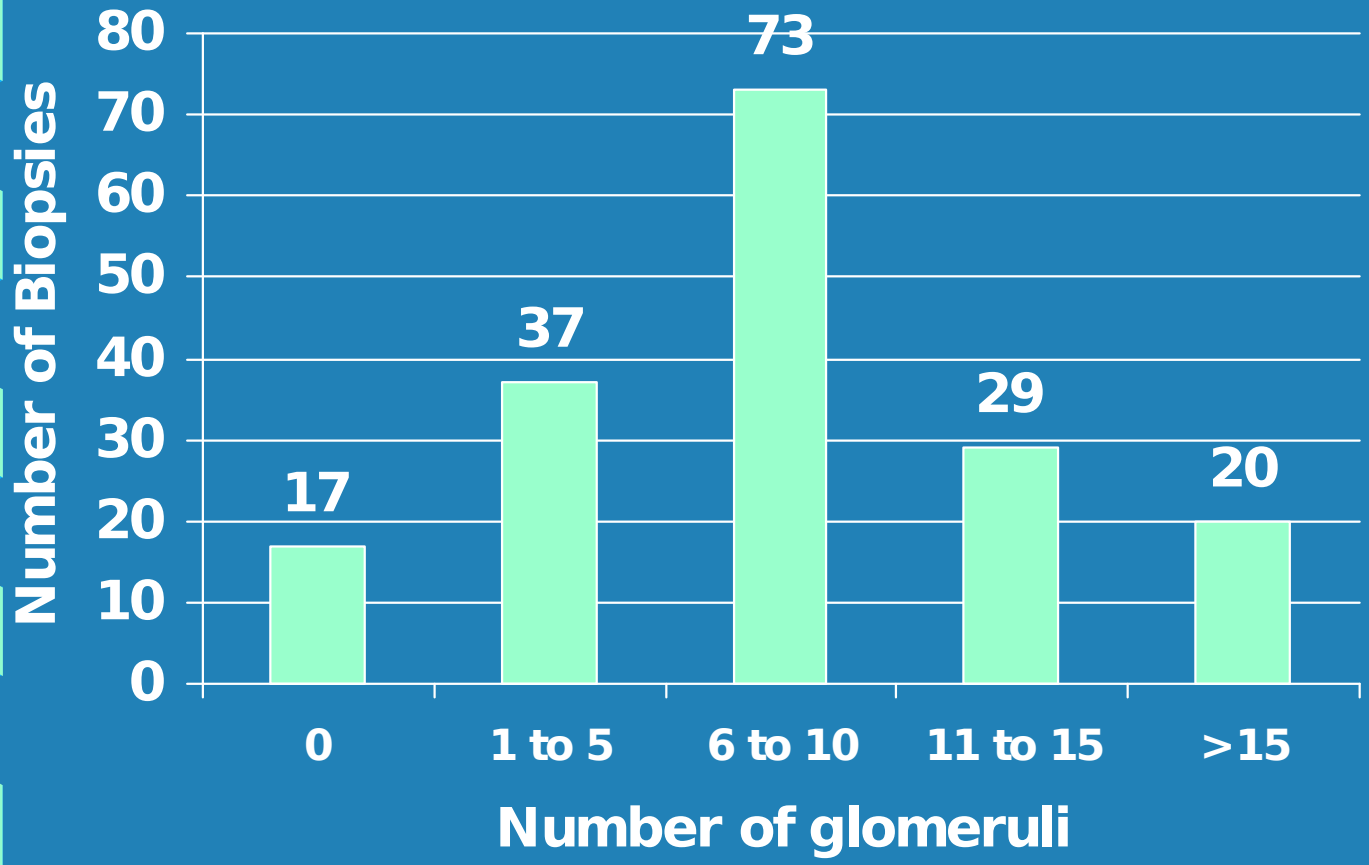
Transjugular renal biopsy

- However, liver biopsy set was inadequate, modified into the following:
  - catheter length 62.5 cm, gauge 9F, precurved 45°
  - needle length 63.8 cm, gauge 15 G (1.84 mm), with reversed bevel at 45°
  - 1 cc of contrast (Telebrix 38) mixed with 1 cc of saline used to check needle placement
  - max of 3 passes

Transjugular renal biopsy

- Tissue obtained in 88%, with diagnostic utility in 83%.
- 6/200 (3%) received transfusions
- 15/200 (7.5%) had gross hematuria.
- 10/200 (5%) had perirenal hematomas, four req transfusions
- No deaths.

Transjugular renal biopsy



Transjugular renal biopsy

- Summary of role for transjugular biopsy:
  - Strong indication:
    - Bleeding disorders preventing conventional biopsy
    - Poro background representing vital risk in the event of biopsy complications req surgery
    - Patients with mechanical ventilatory assistance.

Transjugular renal biopsy

- Based on a follow-up study of 70 patients (1), an additional strong indication is need for combined liver and kidney biopsy, usually in preparation for orthotopic liver transplant (which may be in a setting of hepatorenal syndrome).

Transjugular renal biopsy

- Possible indication:
  - patients enrolled in prospective trials requiring multiple biopsies
  - solitary right (NOT left) kidney

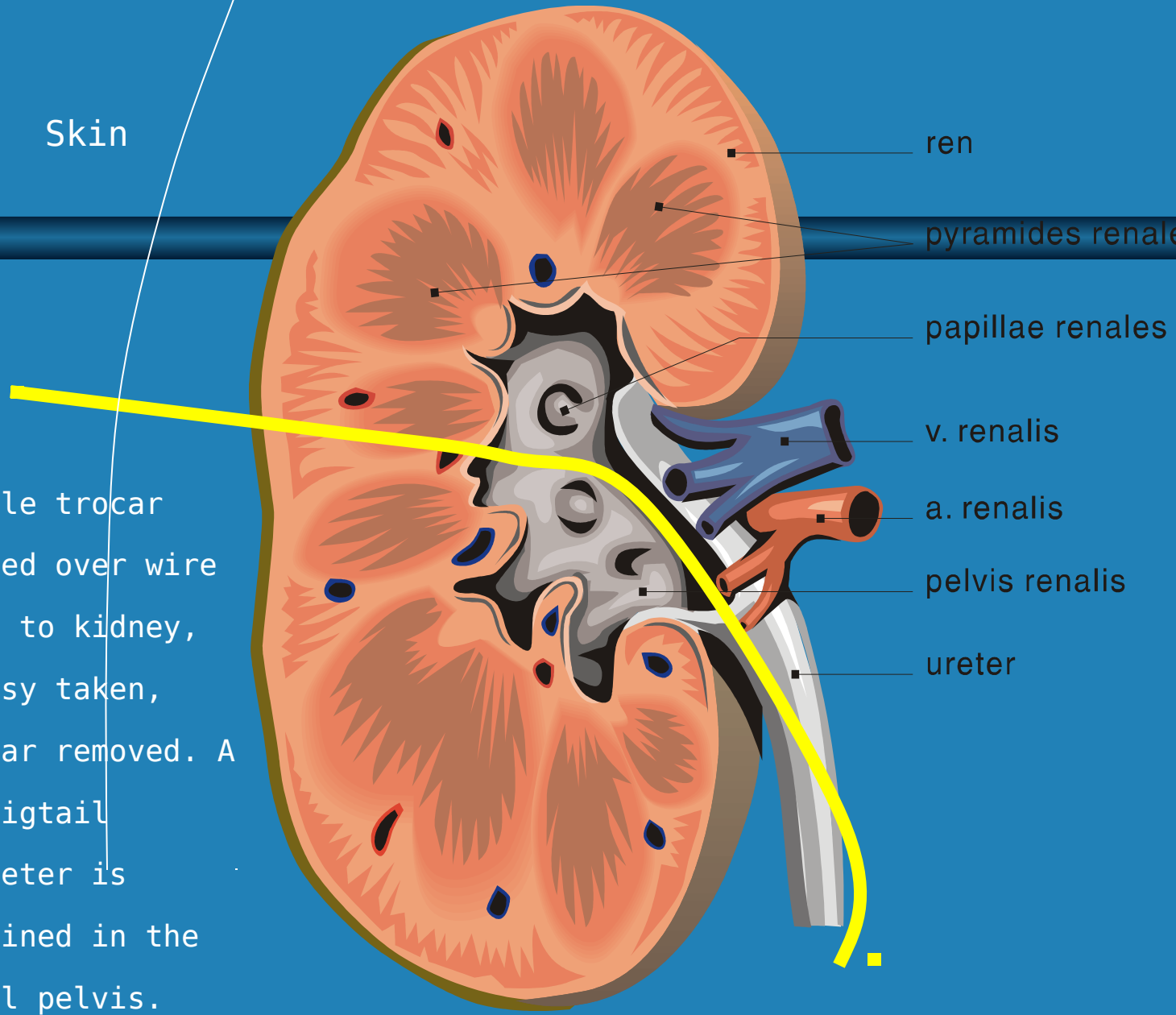
Transjugular renal biopsy

- Poor indication:
  - small, contracted kidneys (capsule <2 cm from needle site)
  - thrombosis of inferior vena cava, right renal vein, thrombosis or congenital absence of right internal jugular vein, or recurrent course of right renal vein.
  - Dilated urinary tract and thin renal cortex

Renal Needle biopsy along the retrograde puncture line of the renal calyx

- In another type of biopsy, a catheter is inserted up the bladder, ureter and into the renal pelvis and then punctures through the capsule and out through the skin in the manner of a nephrostomy.

Skin



Needle trocar fitted over wire down to kidney, biopsy taken, trocar removed. A 7F pigtail catheter is retained in the renal pelvis.

Laparoscopic renal biopsy

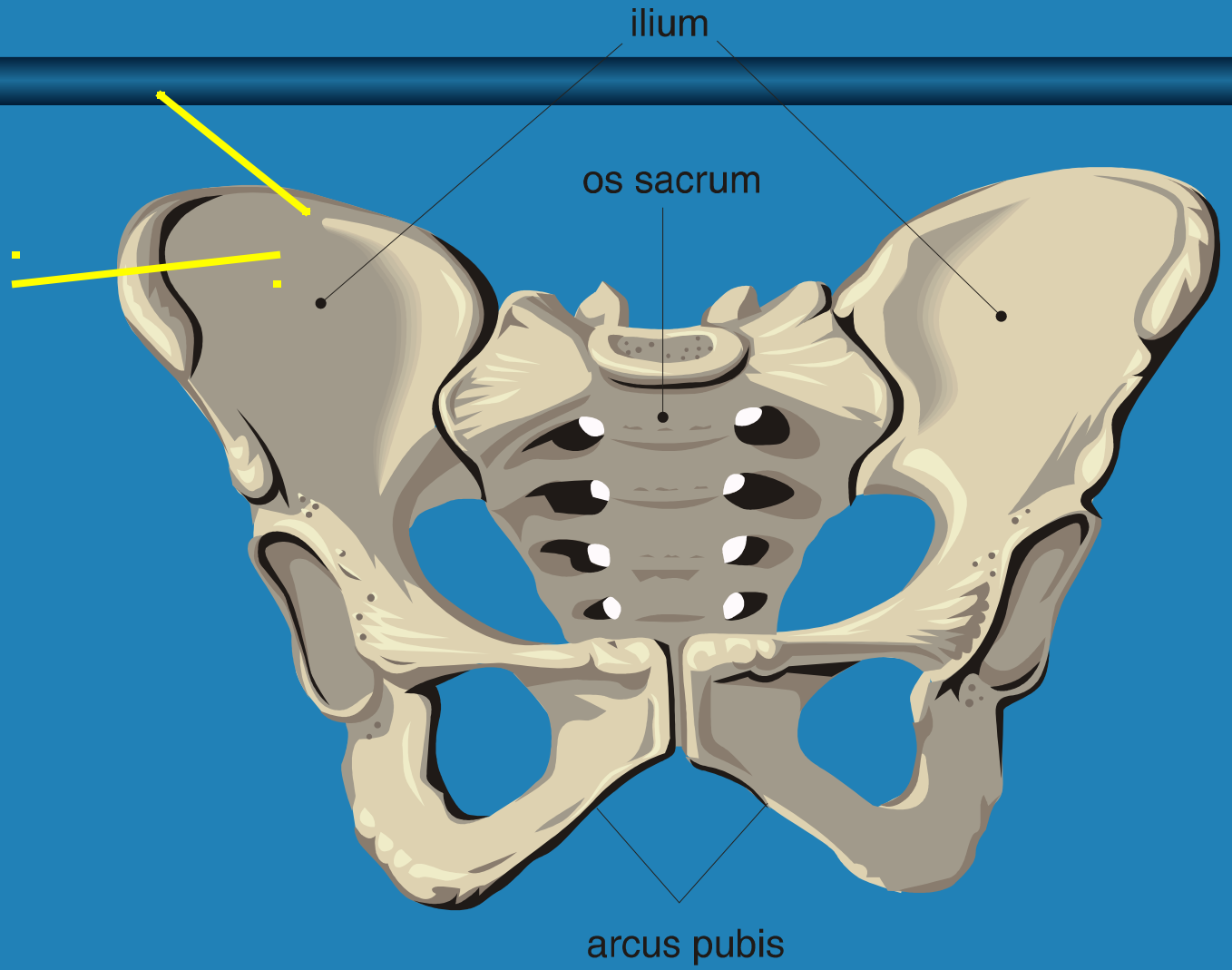
- Case series of 32 patients (21 women, 11 men) at Johns Hopkins, felt to be unsuitable candidates for PRB (morbid obesity, solitary kidney, religious reasons, or chronic anticoagulation.
- Sample pictures of laparoscopy at laparoscopy.com

Laparoscopic renal biopsy

- Indications for laparoscopic biopsy
  - Failed percutaneous renal biopsy
  - chronic anticoagulation/coagulopathy
  - morbid obesity
  - solitary kidney
  - religious (Jehovah's Witness)
  - multiple bilateral renal cysts
  - body habitus (cerbral palsy)

Laparoscopic renal biopsy

- General anesthesia
- Two port technique via retroperitoneal route
  - 10 mm port placed above iliac crest in posterior axillary line
  - 5 mm port placed at the same level in the anterior axillary line, except in the morbidly obese patient placed under direct vision.


ilium
os sacrum
arcus pubis

Laparoscopic renal biopsy

- Incision size <1 cm
- After air inserted, minimal blunt dissection through retroperitoneal fat exposed lower pole of kidney.
- Laparoscopic cup forceps used to take multiple superficial cortical biopsies.

Laparoscopic renal biopsy

- Biopsy site fulgurated with an argon beam coagulator and a sheet of oxidized cellulose.
- OR time was 1.5 hrs (0.8-3.0 hrs)
- Results: All biopsies had adequate tissue. Mean EBL was 26 cc (range, 5-100).
- Avg hospital stay 1.7 d (0-7)

Laparoscopic renal biopsy

- Half (16) of the patients were DC'd on the day of the procedure
- Six patients were DC'd after an overnight stay
- Eight req longer stays for unrelated reasons
- Average return to normal activity in 1.7 weeks (0.3-3.0)

Laparoscopic renal biopsy

- Tissue adequacy was 100% (# of glomeruli not stated) using the cup biopsy forceps (NOT core needle)
- In one case, the spleen was inadvertently biopsied but promptly recognized and hemostasis achieved.

Laparoscopic renal biopsy

- One death occurred related to high dose steroid therapy for lupus nephritis (perforated gastric ulcer one week later, refused blood transfusions for religious reasons).
- Long-term follow-up lacking.

Comparison of most frequently described techniques

	General Anesthesia	Adequacy	Morbidity	Complexity, Cost
Open	Y	3	3	3
Laparoscopic	Y	3	1	2
Transjugular	N	1	1	1
Percutaneous	N	2	2	0

Relative scale, 0-3 scale, 0 lowest, 3 highest

Approach to high risk patients: medical

- For patients with minor coagulopathies, coagulation products can be given before and after the time of biopsy.
- However, the period of risk extends for 6 weeks after biopsy.
- For the management of uremic bleeding, please see our lecture of the same name

Approach to high risk patients: medical: hemostatic agents

Table 1. Available Products (Anon, 1988; Huff, 1988; Lampe, 1986; Seinyard & Pathak, 1985; Huff, 1988a; Huff, 1988b)

Material/Product Name	Manufacturer
Gelatin, Absorbable	
-Gelfoam(R) (sponge, powder)	Upjohn
-Gelfilm(R) (film)	Upjohn
Oxidized Cellulose	
-Oxycel(R)	Park-Davis
-Hemopak(R)	Johnson & Johnson
Oxidized Cellulose, Regenerated	
-Surgicel(R)	Johnson & Johnson
-Surgicel, Nu-Kint(R)	Johnson & Johnson
Absorbable Collagen Sponge	
-Collastat(R)	Kendall
-Helistat(R)	Marion
-Hemopad(R)	Astra
-Instat(R) (sponge-like pad)	Johnson & Johnson
Microfibrillar Collagen	
-Avitene(R) (powder/non-woven web sheet)	Alcon

Approach to high risk patients: medical: hemostatic agents

- Absorbable gelatin is obtained from denatured animal skin gelatin (Schwartz et al, 1979).
- Used alone, this product possesses no coagulating properties, however, the hemostatic actions can be produced when it is used in combination with topical thrombin. Along with thrombin, which is used to initiate coagulation, the large surface area of the gelatin product acts to absorb blood and exert weight on the hemorrhaging area (Schwartz et al, 1979).
- These purified gelatin products are capable of absorbing up to 45 times their weight in blood (Arand & Sawaya, 1986).

Approach to high risk patients: medical: hemostatic agents

- Most cases in literature report on use in arterial puncture sites.
- No human cases on use in renal biopsies.
- A few reports on use of steel coil embolization and gelfoam in liver biopsy patients (see references below) and are proposed as alternatives to the transjugular approach.

Approach to high risk patients: medical

- A report on use of a Type I collagen expandable hemostatic plug (bovine collagen) in a swine kidney biopsy model (1).
- 3000 u heparin given IV
- 14 G Temno coaxial needle used in performing 9 pairs of renal biopsies

Approach to high risk patients: medical: hemostatic agents

- For control biopsies, the trocar system was removed after biopsy.
- For the test biopsies, the plug delivery system was immediately inserted into the outer coaxial trocar to a depth equal to the length of the trocar.
- One test site failed due to kinking.

Approach to high risk patients: medical: hemostatic agents

- Trocar was then pulled out, and a custom designed push rod was held firmly while the sheath containing collagen plug was retraced, exposing the collagen plug at the biopsy site.
- Results: Statistically significant decreases in bleeding frequency, duration, and intensity.

Approach to high risk patients: medical: hemostatic agents

- Caution is warranted, however. Use of similar collage plugs for femoral artery closure resulted in complication rates of >30% (1).

Conclusions

- The patient at high risk for percutaneous renal biopsy can now be approached by a variety of techniques, both procedural and medical, to minimize bleeding and other complications

Conclusions (Cont'd)

- Solitary kidney is now only a relative contraindication
  - Some authors would still perform percutaneous biopsy, others would refer for transvenous or laparoscopic if available, or open biopsy.

Conclusions (Cont'd)

- Patients with liver disease needing a combined liver and kidney biopsy would be best served with a transjugular biopsy currently--combined laparoscopic liver and kidney biopsy has not yet been described.

Conclusions (Cont'd)

- Patients with uncorrectable coagulopathy could be referred either for transjugular, laparoscopic or open biopsy
- Patient with atrophic kidneys at ESRD would best be approached by laparoscopic or open biopsy, if biopsy is truly indicated.